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The Role of Slit2 in Lung Cancer Cell Growth and Invasion Inhibition

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The expression of slit2 is highly repressed in lung cancer. Slit2 is a secreted protein and is known to function as a chemorepellent in axon guidance and neuronal migration. Recent studies showed that slit2 promoter is hypermethylated in several human cancers and it may act as a tumor suppressor however other report showed that slit2 can induce angiogenesis. Therefore, the role of slit2 in carcinogenesis remains to be clarified. While the expression of Slit2 is very low in most of the lung cancer cell lines, it reveals interesting expression pattern in CL1 series cell lines which possesses various invasive abilities. The expression of Slit2 is high in a low invasive cell line-CL1-0, and very low in high invasive CL1-5 cells. An alternative splice form of Slit2 that deleted exon15 was present in all lung cancer cell lines and lung tissues tested. To study the role of Slit2 in lung cancer, full-length cDNA clones containing exon15 (slit2-WT) or deleting exon15 (slit2-ΔE15) were constructed. Our studies showed that slit2-ΔE15 reduced cell growth in CL1-5 cells, while slit2-WT had no effect on cell growth. Slit2-ΔE15 mediated growth inhibition is through Robo1 and Robo4 as evidence by si-Robo1 and si-Robo4 blocks slit2-ΔE15 mediated growth inhibition. Regardless of exon 15 status, both slit2-WT and slit2-ΔE15 decreased in vitro invasive ability of CL1-5 cells. Although both Slit2-ΔE15 and Slit2-WT possess cell invasion inhibition capacity, they function through different receptors. Robo4 is involved in Slit2-WT-mediated cell invasion inhibition but neither Robo1 nor Robo4 is involved in Slit2-ΔE15-mediated invasion inhibition. We speculate that exon 15 may modulates Slit2 function by affecting its affinity to various receptor proteins.

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Profiling Low Abundant Somatic Mitochondrial DNA Variations in Colorectal Cancer by Next Generation Sequencing

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Mitochondrial DNA mutations are associated with tumorigenesis and progression of several cancers. However, the study of mitochondrial DNA mutation is difficult because there are thousands of copies of mitochondrial genomes in a cell and they are heteroplasmic. In this study, we introduced a method using next generation sequencing to profile mitochondiral DNA variations, and used this method to identify the variations that are enriched in colorectal cancer. Paired normal and tumor tissues from two colorectal cancer patients were subjected to RNA extraction and high throughput sequencing with Illumina Solexa sequencer. The sequences were aligned to mitochondrial genome using the software Seqmap. Variations that were enriched for more than 2 folds were then identified with the software Mapview and MySQL. Around 2 million reads for each sample could be mapped to mitochondrial genome, covering almost all coding regions but not tRNA genes or non-coding regions. Seventeen non-synonymous mutations in 8 genes were enriched in cancer tissues, including mt-atp6, mt-co2, mt-co3, mt-nd1, mt-nd4, mt-nd4l, mt-nd5, and mt-nd6. Frequency of these variations ranged from 0.8% to 3.4%, which is difficult to detect using conventional methods. We conclude that next generation sequencing is a powerful tool for the study of mitochondrial mutation.

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Identification of Key Oncogenes Involved in Bladder Cancer Development by Genomewide Analyses

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Bladder cancer is one of the most common cancers of the urinary tract worldwide. Although several oncogenes have been identified in bladder cancer, it is still a challenging task to develop new treatments without a genomic scope of the disease. Given the significant clinical impact of oncogenes, identification and characterization of new oncogenes promise to advance the progress in clinical management of cancer patients. In this study, we performed genotyping on 60 fresh clinical samples by using a 250K single-nucleotide polymorphism array (affymetrix) to detect the alterations of copy number in chromosome. An amplification region was found at 20q11.2 with high frequency of 15% (9 out of 60 bladder cancer tissues). Comparative analyses between genetic alterations and gene transcriptome revealed several oncogene candidates within this amplicon. The findings and impact of this study will be discussed.